DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12-30-08 has been entered.

Claims 1-9, 15, 16 and 18-20 have been canceled. Claims 10-13 and 17 remain pending and under consideration.

Applicant's arguments filed 1-4-09 have been fully considered but they are not persuasive. Please separate arguments for each rejection with a heading. Arguments may be repeated or referred to under each heading; however, all arguments for each rejection must at least be referred to under each heading.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Indefiniteness

The rejection regarding the metes and bounds of “conversion” in claim 10 has been withdrawn because the term has been deleted.

The rejection regarding “pseudo” in claims 15 and 18 has been withdrawn because the term has been deleted.

The rejection of claim 16 has been withdrawn because the claim has been canceled.

Claim Rejections - 35 USC § 102

Claims 10-14 and 17 remain rejected under 35 U.S.C. 102(e) as being anticipated by Rapp (Patent Application Publication US 2002/0108132 A1) for reasons of record.

Rapp taught a chimeric chicken whose genome comprised a transgene encoding a human heavy and/or light chain antibody comprising the V, D, C and J regions (paragraphs 63, 76, 151, 154, 161, 163).

Claim 10 is included because the B cells of the chicken inherently undergo immunoglobulin gene rearrangement (class "switching") and yield isotype G immunoglobulin molecules. Without evidence to the contrary, the transgene taught by Rapp is capable of undergoing rearrangement or switching as claimed because the transgene of Rapp inherently encoded a switch region along with the human Ig heavy and light chains. Accordingly, the Ig produced by the chicken is inherently rearranged and has at least a portion of human Ig as claimed.

The phrase "wherein a population of B lymphocytes produced by the chicken are comprised of rearranged immunoglobulin genes that encode at least a portion of human heavy or light chain immunoglobulin molecule" in claim 10 is also included because the transgene taught by Rapp is equivalent to the transgene claimed because it comprises human Ig heavy and light chains and a switch region making it inherently capable of undergoing rearrangement (switching) as claimed.

Rapp described making a knock-in transgenic chicken in paragraphs 80 and 121, which is equivalent to the chimeric chicken expressing a rearranged Ig gene that encodes at least a portion of human Ig and whose genome has a disrupted endogenous Ig gene as in claim 10 as now amended. The teachings in the specification regarding making knock-in chickens are no greater than those described by Rapp; therefore, Rapp must be applied as art. If applicants show Rapp is not enabled for a knock-in chicken, then the specification as originally filed is not enabled for a knock-in chicken because it has no greater guidance than the teachings of Rapp.

Claims 12-14 are included because the transgene may comprise a plurality of heavy or light chain V or D regions (paragraph 154).

Claim 17 is included because the antibody was expressed in the yolk of an egg produced by the chicken (paragraph 108).

Response to Arguments

Applicants argue Rapp does not enable making a knock-in chicken as now required in claim 10 ("whose genome further comprised of a disrupted endogenous immunoglobulin gene"). Applicants' argument is not persuasive. Rapp described making a knock-in transgenic chicken in paragraphs 80 and 121, which is equivalent to the chimeric chicken expressing a rearranged Ig gene that encodes at least a portion of human Ig and whose genome has a disrupted endogenous Ig gene as in claim 10 as now amended. The teachings in the specification regarding making knock-in chickens are no greater than those described by Rapp; therefore, Rapp must be applied as art. If applicants show Rapp is not enabled for a knock-in chicken, then the specification as

originally filed is not enabled for a knock-in chicken because it has no greater guidance than the teachings of Rapp.

Applicants cite case law regarding inherency but do not elaborate on how the case law applies to the rejection or the claims. Inherency relates to the chicken of Rapp having B cells comprising rearranged Ig genes that encode at least a portion of human Ig heavy or light chain but does not relate to the making knock-in chickens (as implied in the paragraph bridging pg 4-5 of applicants' arguments filed 1-4-10). In this case, the B cells of the chicken inherently undergo immunoglobulin gene rearrangement (class "switching") and yield isotype G immunoglobulin molecules because the transgene of Rapp encodes a switch region along with the human Ig heavy and light chains. Accordingly, the Ig produced by the chicken is inherently rearranged and has at least a portion of human Ig as claimed. The phrase "wherein a population of B lymphocytes produced by the chicken are comprised of rearranged immunoglobulin genes that encode at least a portion of human heavy or light chain immunoglobulin molecule" in claim 10 is also included because the transgene taught by Rapp is equivalent to the transgene claimed because it comprises human Ig heavy and light chains and a switch region making it inherently capable of undergoing rearrangement (switching) as claimed.

Claims 10-14 and 17 remain rejected under 35 U.S.C. 102(e) as being anticipated by Buelow (US Patent 7129084) for reasons of record.

Buelow taught a vector encoding human variable, joining and diversity immunoglobulin genes capable of replacing endogenous immunoglobulin variable, joining and diversity regions. Specifically Buelow taught a BAC vector with a chicken light chain modified by homologous recombination (Fig. 13-15). The vectors are used to make knock-in chickens expressing human variable and joining regions of an immunoglobulin gene (Examples 12-14). The vectors inherently comprise B cell specific regulatory regions operably linked to the human immunoglobulin gene (claim 19) because they are linked to the endogenous chicken heavy chain gene (col. 26, Example 11). Chimeric chickens were obtained (col. 27, line 44). Without evidence to the contrary, the human Ig genes inherently undergo "conversion" or "switching" as claimed because they comprise switch regions.

Response to arguments

Applicants argue Buelow is limited to retroviruses which would not enable the claimed invention. Applicants' argument is not persuasive. Fig. 13 and Example 12 (col. 27, line 38) described using linearized genomic BAC clones modified by homologous recombination to make transgenic chickens. BAC is a bacterial artificial chromosome which is not limited to transferring 10-15 kb fragments.

Claims 10-14 and 17 remain rejected under 35 U.S.C. 102(e) as being anticipated by Singh (US Patent Application Publication 2002/0028488) for reasons of record.

Singh taught a vector encoding human variable, joining and diversity immunoglobulin genes capable of replacing endogenous immunoglobulin variable, joining and diversity regions. Specifically Singh taught a vector with a chicken light and heavy chain modified by homologous recombination (Fig. 2-4). The vectors are used to make knock-in chickens expressing human variable and joining regions of an immunoglobulin gene. The vectors inherently comprise B cell specific regulatory regions operably linked to the human immunoglobulin gene (claim 19) because they are linked to the endogenous chicken heavy or light chain gene (pg 8, paragraph 84). Without evidence to the contrary, the human Ig genes inherently undergo "conversion" or "switching" as claimed because they comprise switch regions.

Applicants argue the Singh publication is a farce. Applicants' argument is not persuasive. Singh taught the method steps required to obtain the chimeric chicken claimed.

Double Patenting

Claims 10-14 and 17 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 11/062325 for reasons of record. Claim 8-11 of '325 are drawn to a genetically modified chicken expressing in tubular gland cells monoclonal antibodies encoded by an exogenous polynucleotide, wherein the monoclonal antibodies are present in egg white at a concentration of at least 40 .mu.g/ml. The product claimed in '325 is an obvious variant of the product claimed in the instant application and is described in the instant disclosure. The product claimed in this application is obvious in

view of the claims of '089 taken with the disclosure of '089. This is a provisional obviousness-type double patenting rejection.

The provisional rejection of claims 10-18 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 10/524089 for reasons of record has been withdrawn because '089 has been abandoned.

Claims 10-14 and 17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9-10 of US Patent 7,323,618 (Application No. 10/216098) for reasons of record. Claim 9-10 of '618 are drawn to a chimeric chicken selectively expressing exogenous protein in tubular gland cells, wherein the exogenous protein is encoded by a transgene stably integrated into a genome of a donor embryonic stem cell whose progeny contribute to the chimeric chicken, and wherein the transgene is greater than 15 kb in size and is comprised of an at least a 7.5 kb portion of an ovalbumin promoter operably linked to DNA encoding the exogenous protein. The product claimed in '098 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '618. The product claimed in this application is obvious in view of the claims of '098 taken with the disclosure of '098. This is a provisional obviousness-type double patenting rejection.

Claims 10-14 and 17 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7 and 9 of US Patent 6,861,572 for reasons of record. Claim 1, 7 and 9 of '572 are drawn to an egg-laying chicken whose somatic cells contain an expression system comprising (i) a first

DNA sequence encoding a human gamma isotype immunoglobulin constant region having a CH2-CH3 region in an Fc domain of the constant region; (ii) a second DNA sequence encoding a human immunoglobulin variable region; (iii) a third DNA sequence comprising an immunoglobulin-gene derived promoter sufficient for expression of the human immunoglobulin constant region in the chicken; wherein the egg-laying chicken produces eggs whose yolk contains human gamma isotype immunoglobulin having a constant region encoded by the first DNA sequence and a variable region encoded by the second DNA sequence. The product claimed in '572 is an obvious variant of the product claimed in the instant application and is described in the disclosure of '572. The product claimed in this application is obvious in view of the claims of '572 taken with the disclosure of '572.

The objection to claim 12 under 37 CFR 1.75 as being a substantial duplicate of claim 14 has been withdrawn because claim 14 has been canceled.

Applicants have not responded to any of the double patenting rejections.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Primary Patent Examiner